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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/652,334	PELTZ ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-41* is/are pending in the application.

4a) Of the above claim(s) *5,6 and 9-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *8/28/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/17/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 5-41 are pending.

Applicant's election with traverse of Group IV, claims 7-8 drawn to a multiprotein complex, in a communication filed on 6/28/2004 is acknowledged.

Applicant's traverse is on the grounds that at least Groups I-XVI are linked by the novel and inventive concept of MTT1 as a modulator of translation termination. As such, Applicants request reconsideration and examination of claims 5-31. Applicants also argue that performing a complete search of any one of Groups I-XVI would also result in a search of Group XVII due to overlapping subject matter. Therefore, it is Applicant's contention that a search of all pending claims would not impose an undue burden of search on the Examiner.

Applicant's arguments have been fully considered but are not deemed persuasive to withdrawn the restriction requirement. The Examiner acknowledges the general subject matter to which Groups I-XVII belong. However, even if one were to assume that the Groups are linked by MTT1, it is noted that the inventions are still distinct from each other for the reasons set forth in the previous Office Action. Furthermore, the Examiner disagrees with Applicant's contention that a search of all the claimed inventions would not impose an undue burden on the Office. A comprehensive search of all groups will require patented/non-patented literature searches, class/subclass searches, and in some cases, sequence searches. These searches may not be overlapping, therefore, a search of all the groups would impose an undue burden on the Office.

The requirement is deemed proper and therefore is made FINAL.

Claims 5-6 and 9-41 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 7-8 are being examined herein.

Specification

1. The specification is objected for not complying with sequence rules. While Figures 1A-1B display alignments of several sequences, neither the drawings nor the Brief Description of the Drawings indicate the corresponding sequence identifiers. Applicant is required to insert the appropriate sequence identifiers in the Brief Description of the Drawings or amend the drawings to include the sequence identifiers in front of each sequence. See particularly 37 CFR 1.821(d). Appropriate correction is required.

2. The abstract of the disclosure is objected to because it should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. Correction is required. See MPEP § 608.01(b).

Priority

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/093,685 filed on 07/22/1998

4. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 09/359,268 filed on 07/22/1999.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 2/17/2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Objections

6. Claims 7-8 are objected to due to the recitation of "Upf1p", "eRF1", "eRF3", "Upf3p" and "Upf2p". Abbreviations unless otherwise obvious and/or commonly used in the art, should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. Appropriate correction is required. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 7-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 7 (claim 8 dependent thereon) are indefinite in the recitation of "MTT1" for the following reasons. While the specification discloses that MTT1 stands for "modulator of translation termination" and also discloses that S. cerevisiae helicase B has been renamed modulator of translation termination (MTT1) by Applicants (page 56, line 28), the specification also discloses that that the MTT1 gene encodes a superfamily group I helicase (page 4, lines 5-7). As such, it is unclear if the modulator of translation termination recited in the claims is a helicase B or any group I helicase. It is suggested that if Applicants wish to recite MTT1, the claims be amended to clearly state that MTT1 refers to helicase B in addition to the recitation of the term "modulator of translation termination". For examination purposes, the term "MTT1" will be interpreted as "helicase B". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 7-8 are directed to a multiprotein complex comprising a genus of helicase B proteins, a genus of human Upf1p, a genus of peptidyl eucaryotic factor 1 (eRF1) proteins, a genus of peptidyl eucaryotic factor 3 (eRF3) proteins, a genus of human Upf2p proteins, and a genus of human Upf3p proteins, wherein the complex is effective in modulating peptidyl transferase activity during translation. While the specification discloses the structure of the S. cerevisiae helicase B protein, its role in translation termination, its structural similarity with S. cerevisiae Upf1p, and its interaction with S. cerevisiae eRF3, the specification is completely silent in regard to the structures of other helicase B proteins or peptidyl eucaryotic factors from other sources. Furthermore, the specification is silent in regard to the structures of all human Upf proteins required by the claims.

The genus of polypeptides required to make the multiprotein complex is a large, structurally variable genus. While a sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus., in the instant case, there is no structural feature which is representative of all the members of the genus of proteins recited in the claims. Furthermore, while one could argue that the recited genus of polypeptides is adequately described

by the structure of the S. cerevisiae helicase B protein disclosed in Figure 1 and other structures known in the art since one could apply structural homology to isolate other functional homologs as required by the claims, it is noted that the art teaches the unpredictability of using structural homology to accurately determine function and even a high degree of structural homology may not result in functional homology. Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Therefore, in the absence of any additional information correlating structure with the desired function in each of the components of the complex, or any correlation between the structures disclosed and the desired function, many structurally unrelated polypeptides are encompassed by the genus. It is noted that while the claimed multiprotein complex also requires a more limited genus of proteins, i.e. human Upf1p, Upf2p, and Upf3p, the specification provides no teaching as to the structures of these human proteins nor is there any disclosure of the structural elements which are common to all human Upf1p, Upf2p, and Upf3p proteins. As taught by the art, human proteins can have many isoforms. See for example, the teachings of Serin et al. (Molecular and Cellular Biology 21(1):209-223, 2001) in regard to the existence of many isoforms of the human Upf3 protein (Abstract).

In addition, even if all the components of the multiprotein complex were adequately described, it is unclear as to whether the combination of proteins from different sources when assembled will have the desired activity, i.e. modulation of peptidyl transferase activity. No working example has been provided which indicates that a multiprotein complex which combines the human proteins required with those proteins from any organism recited in the claims would

result in a complex effective in modulation of peptidyl transferase activity. The teachings of the specification are deemed insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the genus of polypeptides required to make the claimed multiprotein complex. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

12. Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a multiprotein complex comprising the S. cerevisiae helicase B, S. cerevisiae eRF1, S. cerevisiae eRF3, S. cerevisiae Upf1p, S. cerevisiae Upf2p and S. cerevisiae Upf3p, does not reasonably provide enablement for a multiprotein complex comprising any helicase B, any peptidyl eucaryotic release factor 1-3, any human Upf1p, any human Upf2, or any human Upf3 protein, wherein the complex is able to modulate peptidyl transferase activity during translation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims is not commensurate with the enablement provided in regard to the large number of helicase B proteins, Upf proteins, and peptidyl eucaryotic release factors of unknown structure required in the complex, as well as the lack of knowledge in regard to which of the proteins from any source recited in the claim will form a protein complex with the human proteins required to obtain a complex with the desired activity, i.e. modulation of peptidyl

transferase activity during translation. As indicated above, the specification is completely silent in regard to (1) the structures of the polypeptides required in the complex with the exception of the S. cerevisiae helicase B protein, (2) the structural elements which should be present in all the proteins required such that they display the recited function, i.e. helicase B, peptidyl eucaryotic factor, and Upf, or (3) the structural elements which should be present in all the helicase B proteins and peptidyl eucaryotic release factors such that when combined with the human Upf proteins, they can form a complex which is effective in modulating peptidyl transferase activity. Also, as previously indicated, there is no teaching or working example which would suggest that combining proteins of different sources with the human proteins required will result in a multiprotein complex with the ability to modulate peptidyl transferase activity during translation. While the argument can be made that the proteins required to make the complex can be obtained by sequence homology using the structures disclosed in the art and those disclosed in the specification, the art teaches that even proteins sharing a high degree of structural homology do not necessarily share the same function. See the teachings of Witkowski et al. and Seffernick et al. discussed above. Furthermore, even if one could isolate all the proteins required in the complex, neither the specification nor the art teaches the structural elements required in those proteins from any organism which can be combined with the human proteins recited to obtained a protein complex with the desired function. Since structure determines function, one of skill in the art would require some knowledge or guidance as to how structure correlates with the function desired. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to display the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to make a multiprotein complex with the functional characteristics required. Thus, Applicant has not

provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Conclusion

13. No claim is in condition for allowance.

14. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

15. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
July 28, 2004